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011604

PHA 4185.3 (3478/1A/US)  
PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of Gilles H. Goetz et al.  
Serial No. To Be Assigned  
Filed January 16, 2004  
Confirmation No. To Be Assigned  
For PROTEASE INHIBITORS OF THE COAGULATION CASCADE ISOLATED  
FROM *DYSIDEA* SPONGES

January 16, 2004

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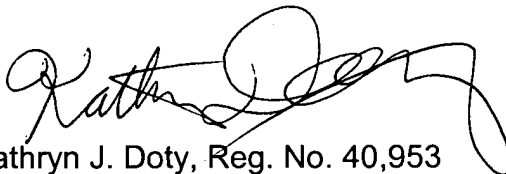
SIR:

**INFORMATION DISCLOSURE STATEMENT**

In accordance with 37 C.F.R. 1.97 and 1.98 and MPEP 609, and in compliance with the duty of disclosure set forth in 37 C.F.R. 1.56, applicants submit the attached PTO/SB/08A, with references listed thereon, for consideration by the Patent and Trademark Office in the above-entitled application and to be made of record therein.

The references listed on the attached PTO/SB/08A have been previously submitted in parent application Serial No. 10/307,803 filed December 2, 2002 and, therefore, in accordance with MPEP 609, are not being provided at this time.

Respectfully submitted,



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KJD/msc  
\*Attachment  
Express Mail Label No. EV 324739113 US

<b>PTO/SB/08A</b>  <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (use as many sheets as necessary)				<b>Complete if Known</b>	
				Application Number	To Be Assigned
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				First Named Inventor	Gilles H. Goetz et al.
				Group Art Unit	Unknown
				Examiner Name	Unknown
Sheet	1	of	3	Attorney Docket No.	PHA 4185.3 (3478/1A/US)

U.S. PATENT DOCUMENTS							
Examiner Initials*	Cite No. <sup>1</sup>	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY		
		Number	Kind Code <sup>2</sup> (if known)				
	1	5,856,309		Konetschny-Rapp et al.	01-05-1999		
	2	6,218,365	B1	Adang et al.	04-17-2001		
FOREIGN PATENT DOCUMENTS							
Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document			Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	T <sup>6</sup>
		Office	Number <sup>4</sup>	Kind Code <sup>2</sup> (if known)			
	3	DE	44 36 772	A1	Boehringer Mannheim GMBH	04-18-1996	A
OTHER ART - NON PATENT LITERATURE DOCUMENTS							
Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.					T <sup>6</sup>
	4	BACHAND et al., "Potent and Selective Bicyclic Lactam Inhibitors of Thrombin. Part 4. Transition State Inhibitors." Bioorg. Med. Chem. Lett, 2001, pp. 287-290, Vol. 11.					
	5	CLAESON, G., "Synthetic Peptides and Peptidomimetics as Substrates and Inhibitors of Thrombin and other Proteases in Blood Coagulation System." Blood Coagulation and Fibrinolysis, 1994, pp. 411-436, Vol. 5.					

Examiner Signature		Date Considered	
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\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup>Unique citation designation number. <sup>2</sup>See attached Kinds of U.S. Patent Documents. <sup>3</sup>Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup>For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup>Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup>Applicant is to place a check mark here if English language Translation is attached or place an "A" here if English language abstract is attached..

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Sheet	2	of	3	Attorney Docket No.	PHA 4185.3 (3478/1A/US)

	6	FUJII et al., "Comparative Study of Toxic and Non-Toxic Cyanobacterial Products: A Novel Glycoside, Suomilide, from Non-toxic Nodularia Spumeigena HKVV." Tetrahedron Lett., 1997, pp. 5529-5532, Vol. 38, No. 31.	
	7	HANDIN, R., "Bleeding and Thrombosis." Harrison's Principles of Internal Medicine, 12th Edition, 1991, pp. 348-353, McGraw-Hill, Inc., New York.	
	8	HARRIGAN et al. "Dysideaprolines A-F and Barbaleucamides A-B, Novel Polychlorinates Compounds from a Dysidea Species." J. Nat. Prod., 2001, pp. 1133-1138, Vol. 64, No. 9.	
	9	ISHIDA et al., "Aeruginosins, Protease Inhibitors from the Cyanobacterium Microcystis Aeruginosa." Tetrahedron, 1999, pp. 10971-10988, Vol. 55, No. 36.	
	10	ITOU et al., "Oscillapeptins A to F, Serine Protease Inhibitors from the Three Strains of Oscillatoria Agardhii." Tetrahedron, 1999, pp. 6871-6882, Vol. 55, No. 22.	
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	12	LEFKOVITS et al., "Direct Thrombin Inhibitors in Cardiovascular Medicine." Circulation, 1994, pp. 1522-1536, Vol. 90, No. 3.	
	13	MAJERUS, et al. "Anticoagulant, Thrombolytic, and Antiplatelet Drugs." Goodman & Gilman's The Pharmacological Basis of Therapeutics, Ninth Edition, 1996, pp. 1341-1359, McGraw-Hill, New York.	
	14	MATSUDA et al., "Aeruginosins 102-A and B, New Thrombin Inhibitor from the Cyanobacterium Microcystis Viridis (NIES-102)." Tetrahedron, 1996, pp. 14501-14506, Vol. 52, No. 46.	
	15	MURAKAMI et al., "Aeruginosin 298-A, A Thrombin and Trypsin Inhibitor From the Blue-Green Alga Microcystis Aeruginosa," Tetrahedron Lett, 1994, pp. 3129-3132, Vol. 35, No. 19.	
	16	MURAKAMI et al., "Aeruginosins 98-A and B, Trypsin Inhibitors from the Blue-Green Alga Microcystis Aeruginosa." Tetrahedron Lett., 1995, pp. 2785-2788, Vol. 36, No. 16.	
	17	RADAU et al., "Synthesis of a Cyanopeptide-analogue with Trypsin Activating Properties." Bioorg. Med. Chem. Lett., 2000, pp. 779-781, Vol. 10.	
	18	RAJ et al. "Long-term Oral Anticoagulant Therapy: Update on Indications, Therapeutic Ranges, and Monitoring." The American Journal of the Medical Sciences, 1994, pp. 128-132, Vol. 307, No. 1.	

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	19	SANDLER et al., "Atomic Structure of the Trypsin-Aeruginosin 98-B Complex." J. Am. Chem. Soc., 1998, pp. 595-596, Vol. 120, No. 3.	
	20	SHIN et al., "Aeruginosins 205A and -B, Serine Protease Inhibitory Glycopeptides from the Cyanobacterium Oscillatoria agardhii (NIES-205)." J. Org. Chem, 1997, pp. 1810-1813, Vol. 62, No. 6.	
	21	STEINER et al., "Structure of Thrombin Inhibited by Aeruginosin 298-A from a Blue-Green Alga." J. Am. Chem. Soc., 1998, pp. 597-598, Vol. 120, No. 3.	
	22	TAPPARELLI et al., "Synthetic Low-Molecular Weight Thrombin Inhibitors: Molecular Design and Pharmacological Profile." Trends in Pharmacological Sciences, 1993, pp. 366-376, Vol. 14.	
	23	VALLS et al., "Total Synthesis and Reassignment of Configuration of Aeruginosin 298-A." J. Am. Chem. Soc., 2000, pp. 11248-11249, Vol. 122, No. 45.	
	24	WEITZ et al., "New Anticoagulant Strategies." Laboratory and Clinical Medicine, 1993, pp. 364-373, Vol. 122, No. 4.	
	25	WIPF et al., "Total Synthesis and Stereochemical Revision of (+)- Aeruginosin 298-A." Org. Lett., 2000, pp. 4213-4216, Vol. 2, No. 26.	
	26	PCT/US02/40001 PCT International Search Report completed May 25, 2003	

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